

### **Remarks**

Claims 1-18 and 27-44 are pending in the application. Claims 1, 2, 5-8, 11, 12, 27, 28, 31-34, 37, and 38 have been amended.

Support for the claim amendments can be found throughout the application, including the claims as originally filed. Importantly, no new matter has been added to the claims. The amendments to the claims should not be construed to be an acquiescence to any of the rejections. The amendments to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants reserve the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Finally, the specification has been amended to include a specific reference to an earlier application from which benefits are being claimed.

### **Priority**

The Examiner noted that a first sentence claiming the benefits of an earlier application was missing from the specification. The Applicants have amended the specification to add a sentence claiming priority to U.S. provisional application 60/156,275, filed September 27, 1999.

### **Claim Rejections Based on 35 USC § 112¶2**

Claims 1, 7, 11, 27, 33, and 37 stand rejected under 35 U.S.C. § 112¶2 based on the Examiner's contention that they are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicants respectfully traverse this rejection.

The Examiner contends that the Applicant "has not addressed the groups hanging on the bivalent acyl, ether, sulfonyl, carbonyl, phosphoryl, amido, ester, etc." Accordingly, the Applicants have amended claims 1, 7, 11, 27, 33, and 37, as well as claims dependent thereon, replacing the terms in question with structural formula that make clear their mono-valent nature and their structural metes and bounds. The Applicants respectfully submit that because these structures correspond to groups

originally presented in the claims, no new matter has been added. Moreover, the Applicants respectfully assert that the amendments made herein do not reflect a decrease in the scope of the invention for which protection is sought.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶2.

#### **Claim Rejections Based on 35 USC § 112¶1**

The Examiner has maintained her rejection of claims 1-18 and 27-44 under 35 U.S.C. § 112¶1 based on her contention that the Specification does not enable a person skilled in the art to which it pertains or with which it is most nearly connected to make and use the invention commensurate in scope with the claims. Specifically, the Examiner acknowledges the preparation of eight compounds, but contends that the Specification is enabling only for these exemplified compounds for inhibition of the reuptake of norepinephrine and epinephrine, thereby rendering only these compounds useful for the treatment of depression, cocaine addiction and other maladies. The Applicants respectfully traverse this rejection.

It is well established in patent law that the Applicants need not prepare and test every compound for desired properties to obtain a patent for those compounds. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. § 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir.), *cert. denied*, 484 U.S. 954 (1987).

The Applicants respectfully submit that they have enabled a representative number of compounds relative to that which is claimed. The compounds of the present claims are described by formula (I). The compounds of formula (I) have a tropane framework and differ by the R and A groups. Therefore, the claims share basic structural

characteristics and differ by substitutions with commonly recognized groups in organic chemistry.

The Examiner states that “[u]ndue experimentation would be required for the skill in the art to make these highly substituted compounds, (where the ring substituents are further substituted by bulky substituents), especially when the starting materials have not been disclosed.” The Examiner alludes to the availability of starting materials as a factor pertinent to enablement. This position is in line with accepted practice as evidenced by the M.P.E.P. § 2164.01(b) which states “[a] key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available.” Importantly, in this regard, to support the position that the specification is adequately enabling, **Exhibits A-D** are submitted with this *Amendment and Response*, showing that certain tropane compounds were available at the time of the filing of the application. These references show that tropane structures with various substituents at the 2-, 3-, 6-, 7-, and 8-positions were in the public domain at the time the instant application was filed.

**Exhibit A:** Newman et al. “Novel 3 $\alpha$ -(Diphenylmethoxy)tropane Analogs: Potent Dopamine Uptake Inhibitors without Cocaine-like Behavioral Profiles” *J. Med. Chem.* **1994**, 37, 2258-2261. Exhibit A shows that ester and alkoxy substitutions were well known at the 2 and 3 position of the tropane skeleton. Therefore, one of ordinary skill in the art of synthetic organic chemistry would be able to prepare tropane analogs with ester and alkoxy substitution at the 2 and 3 position as well as substitutions that can be derived from ester or alkoxyl groups.

**Exhibit B:** Roberts et al. “Self-administration of Cocaine Analogs by Rats” *Psychopharmacology* **1999**, 144, 389-397. Exhibit B shows tropane analogs where the 8 position is substituted with Me; the 2 position is substituted with ketone or ester; and the 3 position is substituted with

ester, aryl, or aralkyl. Therefore, one of ordinary skill in the art of synthetic organic chemistry would be able to prepare tropane analogs with a varied amount of substituents at the 2, 3, and 8 position.

**Exhibit C:** Meltzer et al. U.S. Patent No. 5,948,933. Exhibit C shows tropane analogs where the 2 position is substituted with ester, ketone, alkyl, alkenyl, alkynyl, or amide; the 3 position is substituted with aryl or aryloxy, the 6 and 7 positions are substituted with hydroxy, alkoxy, halide, or amino; and the 8 position is substituted with aralkyl, aryl, alkyl, alkenyl, or alkynyl. Therefore, one of ordinary skill in the art of synthetic organic chemistry would be able to prepare a number of tropane analogs with many different substitutions at the 2, 3, 6, 7, and 8 position.

**Exhibit D:** Newman et al. U.S. Patent No. 5,792,775. Exhibit D shows tropane analogs where the 3 position is substituted with alkoxy groups and the 8 position is substituted with alkyl, formyl, ester, aralkyl, and alkenyl groups. Therefore, one of ordinary skill in the art of synthetic organic chemistry would be able to prepare tropane analogs with a number of substituents at the 3 and 8 positions.

Consequently, the Applicants respectfully contend that given the above combined teachings, tropane substitution chemistry was advanced enough that a number of different tropane analogs existed or could be prepared at the time of filing. Therefore, with reference to the exemplification provided in the instant application, and armed with the contents of the public domain, the Applicants respectfully assert that one of ordinary skill in the art of synthetic organic chemistry would be able to prepare the compounds of the present claims. Limiting the claims to only the compounds prepared would be unfair to the Applicants because, given the level of knowledge of tropane chemistry in the art, one

could easily design around the claims suggested by the Examiner by preparing substituted tropanes not covered by the suggested claims.

The other objection raised by the Examiner is whether the compounds claimed but not prepared have the claimed activities. The Applicants respectfully submit that in accordance with *In re Brana* the Examiner may be confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. *See In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). In *In re Brana*, a compound that was structurally similar to a compound known to have a certain property was held to have the same utility even though it had not been expressly tested for those properties. The court held this view even while acknowledging that “[a]lthough it is true that minor changes in chemical compounds can radically alter their effects on the human body, *Kawai*, 480 F.2d at 891, 178 USPQ at 167, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility. *See Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 USPQ 453 (CCPA 1974); *Kawai*, 480 F.2d 880, 178 USPQ 158.” *Id.* at 1566. As in *In re Brana*, the compounds of the present claims are structurally similar because they share the same basic framework and only differ by the pendant R and A groups. Therefore, testing every compound covered by the present claims for inhibition of reuptake of monoamines should not be a requirement for obtaining a patent.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶1.

**Fees**

The Applicants believe no fee is due in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any required fee to our Deposit Account, 06-1448.

**Conclusion**

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

Respectfully submitted,  
Foley Hoag LLP

By: 

Dana M. Gordon, PhD  
Reg. No. 44,719  
Attorney for Applicants

155 Seaport Boulevard  
Boston, MA 02210  
Telephone: (617) 832-1000  
Telecopier: (617) 832-7000

Date: 7/7/03